Mixed-Effects Analysis of MMSE Variability Across Group and Visits

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Introduction

The Mini-Mental State Examination (MMSE) is a widely recognized tool for evaluating cognitive impairment and tracking changes in cognitive functioning over time. It has been extensively utilized in the assessment of individuals with various neurological conditions, particularly dementia. In clinical and research settings, understanding the factors that influence MMSE scores is crucial for interpreting the progression of cognitive decline and the effectiveness of therapeutic interventions.

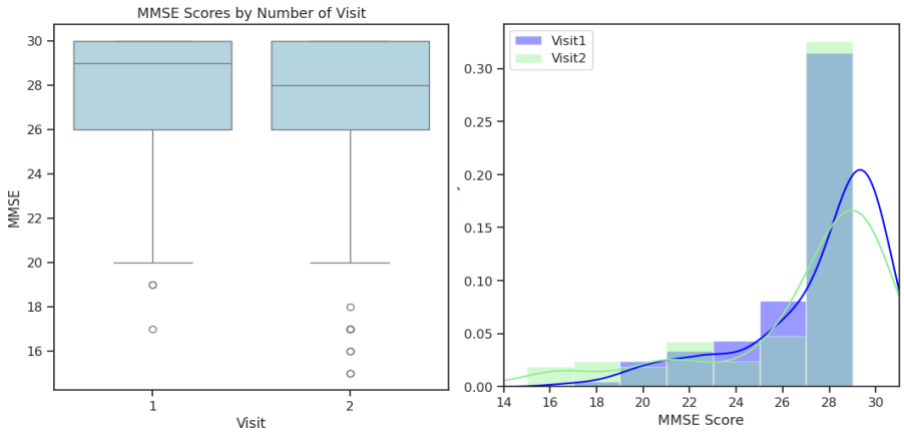
Research Question： whether there are significant main or interaction effects of group categorization and longitudinal measurement frequency on subjects' Mini-Mental State Examination (MMSE) scores.

In MRI studies where MMSE scores are collected over time, mixed-effects ANOVA is ideal for analyzing data because it handles both the consistent factors across all participants (like group status regarding dementia) and individual differences across multiple time points. This analysis helps determine if being in a certain group or the number of measurements taken affects MMSE scores. It can also inform the best timing for cognitive tests and improve interpretation of MMSE changes over time in various patients. The results aim to improve how we monitor cognitive health.

Data Cleaning and Data Wrangling

We prepared the dataset for analysis by first tidying the raw data. We focused on accuracy and reliability, removed errors, and selected relevant columns for our study, creating a new dataset from the original 294 rows and 16 columns. After an initial review, we found minimal missing values and only one missing MMSE score. Considering our dataset's size, we removed this single incomplete entry. With data cleaning complete, we're ready to move on to the next phase of our analysis.

Exploratory Data Analysis (EDA)

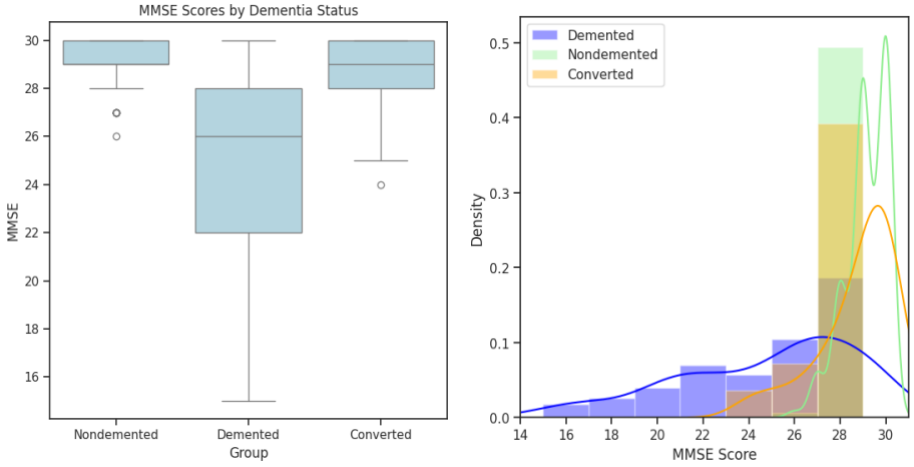


[Figure 1]

To explore whether there are significant main or interaction effects of group categorization and longitudinal measurement frequency on subjects' Mini-Mental State Examination (MMSE) scores, we will first conduct an exploratory analysis of the data. First, we categorized the dataset into two groups based on the number of Visits, the first Visit and the second Visit, and plotted Boxplot and Distribution Plot [Figure 1] for their MMSE results, respectively, to explore trends in their distribution and whether there might be a difference in MMSE scores between the two Visits.

On the left is a box plot showing that in both Visit 1 and Visit 2, the median score is above 25, but the median MMSE in Visit 1 is slightly higher than in Visit 2. However, whether they are significantly different requires follow-up studies. On the right is a distribution plot: Where the histogram shows the frequency distribution of MMSE and the bars represent the number of observations within each score interval. the KDE plot shows a smoothed version of the distribution providing an estimate of the probability density function of the variable. The KDE plot shows the distribution of the MMSE scores for each visit. The histograms and KDE plots for visit 1 (blue) and visit 2 (green) overlap for the most part, suggesting that the overall distribution of MMSE scores did not change significantly from the first visit to the second visit. Figure1 shows that the central tendency and distribution of MMSE scores were relatively stable between visits.

After that, we categorized the dataset into three groups based on the group to which the subjects belonged, i.e., Nondemented, Demented, and Converted, and plotted box plots and distribution plots of their MMSE results, respectively [Figure 2], in order to explore the trend of their distributions and whether there might be a difference in the MMSE scores between the two visits.

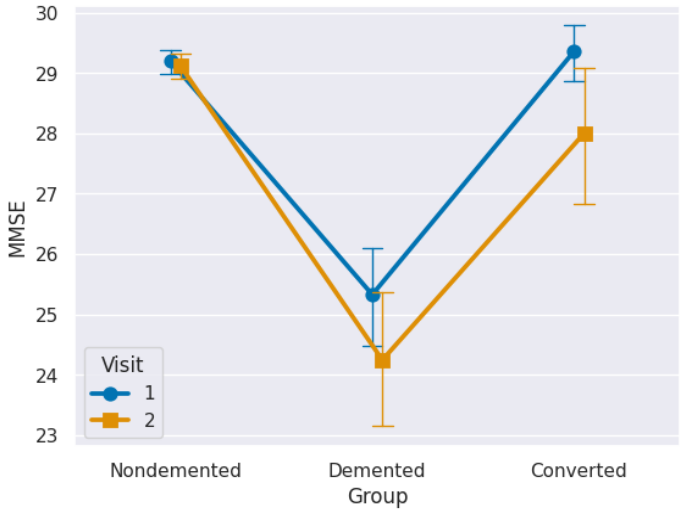


[Figure 2]

The left box plot displays MMSE score distributions across groups categorized by dementia status. The nondemented group exhibits higher median scores with few low outliers, indicating better cognitive health compared to the demented group, which shows lower median scores and more outliers, aligning with the cognitive decline often seen in dementia. The converted group, possibly those transitioning from nondemented to demented, has intermediate scores. The right-side distribution combines histograms and KDE plots, showing that nondemented scores are higher, demented scores are lower and more spread out, and converted scores fall in the middle. Overall, these patterns reflect the expected variations in cognitive abilities among the different groups.

Mix Effect ANOVA Analysis

The Figure 3 displays MMSE scores for three groups (Nondemented, Demented, Converted) across two different visits. There are visible changes in scores between visits within groups, especially in the Demented group, where scores increase on the second visit, and in the Converted group, where scores decrease. This pattern of within-group changes and between-group differences does suggest that a mixed-effects ANOVA could be an appropriate statistical method to analyze the data.



[Figure 3]

Mixed Effect ANOVA was designed to explore the effect of two factors on MMSE scores: number of visits (a within-subject factor indicating repeated measures) and dementia group classification (a between-subject factor). For the number of visits, the null hypothesis (H0) suggested that there was no significant difference in MMSE scores across visits, while the alternative hypothesis (H1) suggested that there was a difference. For the dementia group, the H0 hypothesis assumes that there is no significant difference in MMSE scores between groups, and the H1 hypothesis assumes that there is a difference. The H0 for interaction effects hypothesized that the combination of number of visits and dementia group had no significant effect on MMSE scores, whereas H1 suggested a significant interaction effect.

Source	SS	DF1	DF2	MS	F	p-unc	np2
Group	1328.421	2	140	664.211	56.21	<.001	.445
Visit	22.378	1	140	22.378	8.86	.003	.060
Interaction	17.000	2	140	8.500	3.37	.037	.046

[Table 1]

The ANOVA result summary table [Table 1] shows: The 'Group' factor had a significant effect on MMSE score with an F value of 56.212 and a p value of less than 0.001. The 'visit' factor also had a significant effect on MMSE scores with an F value of 8.859 and a p-value of 0.003. The interaction between 'group' and 'visit' was significant with an F value of 3.365 and a p-value of 0.037, indicating that the effect of visit on MMSE scores varied across groups. The effect size (np2) of the interaction was 0.046, which is relatively small but significant.

In summary, there were significant main effects of group and visit on MMSE scores, as well as significant interaction effects, all of which suggest that there are differences in MMSE scores between groups, between visits, and between groups with different numbers of visits. This calls for further research into the nature of these differences.

Post Hoc Test

Since ANOVA's results can only tell us that there are differences between groups, but not exactly which groups are significantly different, we need to use the post hoc test to identify them. The results of the post hoc show that there is a significant difference between the groups. Post-hoc test shows the MMSE scores between visits showed significant differences, indicating changes in MMSE scores over time. Comparisons between groups (e.g., Converted vs. Demented) showed significant differences, especially between the Converted and Demented groups, suggesting that dementia status was strongly associated with MMSE scores. Interaction effects also showed some significant results, such as a significant difference between the Converted and Demented groups on the first visit, which may indicate different trends over time for different groups.[See code documentation for full post hoc results]

Power Analysis

According to the previous requirement alpha = 0.05, power = 0.91. effect size = 0.7. we need to require the required sample size. $1-\beta = 0.91$ Therefore, beta = 1.34. According to the formula. We can calculate the Sample size/Number needed in each group is about 45.451. to ensure that the power is not less than 0.91, therefore the number of samples in each group should be 46. Power curve analysis [Figure 4] was conducted to understand the effect of sample size on statistical power for an effect size of 0.7. The curve shows that as the sample size increases, so does the power. With 20 samples, power is just below 0.80, which is considered the minimum acceptable level. Approximately 40 samples are needed to achieve a robust power of 0.90. The power approaches 1.00 with around 70 samples, indicating almost certainty in detecting the effect. The calculated sample size of about 45 ensures adequate power for detecting an effect size of 0.7.

[Figure 4]

Conclusion

The main effects of group and number of visits, as well as the interaction effects between these factors, were evident, highlighting the fact that cognitive scores differed not only at different stages of dementia, but also over time. The increase in MMSE scores from the first to the second visit in the dementia group and the decrease in the transformed group highlight the dynamic nature of cognitive change in these populations. These findings affirm the need for individualized monitoring strategies for cognitive impairment and validate the use of mixed-effects models in longitudinal studies to understand disease progression affecting cognitive function. Further research is warranted to delve into the mechanisms behind these differences and to tailor interventions accordingly.